I

GONOCOCCAL ARTHRITIS

WITH OBSERVATIONS BASED ON A SERIES OF 388 CASES

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In the literature on gonococcal arthritis the earliest reference is the record of a case in 1507 by Van Forest. In 1664 Martiniére [1] drew attention to this clinical entity as a complication of gonorrhœa in his " Traité de la Maladie Veneriénne." The first real presentation of the subject was given by Théophile Salle and Swediaur [2] in 1781, who referred to it as " an inflammatory articular infection dependent on gonorrhœa." The earliest description in English medical literature is by Sir Benjamin Brodie,[3] in 1818, although John Hunter refers to it in one of his treatises in 1786, and Astley Cooper in 1806.

With the discovery of the gonococcus by Neisser [4] in 1879, a controversy arose as to whether the same organism was a factor in the production of the arthritis which occurred as a complication in cases of gonorrhœa. In 1830, William Lawrence [5] had drawn attention to the true nature of gonococcal arthritis. In 1883, Pétrone [6] discovered the organism in the joint fluid in two cases. This work was confirmed by others, and in 1894 Hewes [7] isolated the gonococcus from the blood of patients suffering from polyarthritis.

Incidence.—The estimate of Osler [8] is 2·5 per cent. of all cases. Lumb [9] finds the incidence to be 0·5 per cent. in 50,000 cases. Klose,[10] reporting cases in Germany previous to the war, gives the figure as 2 per cent., while during the war he states that it was as high as 10 per cent. Ireland,[11] in reviewing the U.S. Army Medical Records, found 3·03 per cent. in 259,899 cases. Chiari [12] gives the incidence as 3 per cent. in 45,000 cases. Harrison and

Pollock,[13] in 812 cases in the British Army, gave the figure as 1·85 per cent.

In a consecutive series of over 13,000 cases of gonorrhœa in Edinburgh hospitals, there have been 388 cases of arthritis. This gives a percentage figure of 2·91—3·22 per cent. in males and 1·81 per cent. in females. Arthritis is stated to be four to five times as common in men as in women. Thomas,[14] in a series of 107 cases, finds the proportion much larger, and attributes the increased incidence in the male to the long poorly draining urethra, and to the complicated structure of the prostate and vesicles.

Our figures of the incidence, taken as they are from a V.D. clinic, are probably exaggerated because there is a tendency on the part of doctors to send all cases of acute joint complications to hospital; this would increase the percentage figure in our cases.

Age Incidence.—Arthritis may complicate gonorrhœa at any age, but it is more frequent in young men from twenty to thirty years of age, largely because gonorrhœa is more frequent then. In females the same age period holds good. It occurred in the very young in association with ophthalmia neonatorum in two of our cases. Cases of this have been recorded, but are very rare. In a series of 150 cases of vulvo vaginitis in children we had no case of arthritis as a complication. This is not the experience of American workers.

Predisposing Causes.—The most important is lack of treatment in the earlier stages of gonorrhœa. It is noteworthy that arthritis is rare in cases of anterior urethritis in the male and in cases of urethritis in the female. If these cases are treated early and intelligently, the infection rarely passes to the posterior urethra in the male or the cervix in the female. Another predisposing cause is too active exercise or heavy exercise during the acute stage of the disease; not infrequently the patient attributes the joint condition to some trauma. In all cases of gonococcal infection, alcoholism predisposes to metastatic complications, of which arthritis is the most frequent. Arthritis is always prone to recur, and one attack predisposes to a subsequent one. Recurrence of infective manifestations in a joint frequently follows a reinfection or the lighting up of a chronic focus.

Ætiology.—In every case there is a primary focus of

infection in some part of the body ; the genital or urinary tract is the common site, but it may be the conjunctiva or other mucous surface. The infection of the joint is metastatic, and the organism is carried by the blood stream to the affected joint. The gonococcus was first isolated from the blood by Thayer and Blumer.[15] Columbini, and two years later Uysing,[16] demonstrated it in the lymph stream. Zieler [17] believes that all gonorrhœal infections begin as a septicæmia, and that the organisms disappear quickly from the blood stream, or are present in such small numbers as to make it difficult to find them by blood culture. It is interesting to note in this connection that in cases of acute arthritis it is often difficult to find the organisms in joint fluid after a few days. They seem to disappear from any encapsulated fluid after a time. This will be referred to later. There are some mild cases in which it is possible that the arthritis is due to a toxæmia. Lofaro,[18] in an examination of sixty-seven cases of gonorrhœa, found the organism in the blood in thirty-nine of them. The disease was in the subacute or chronic stage in all these cases. He believes that gonococci appear in the blood stream and survive in it only when a virulent strain of bacteria is present, or when the soil is suitable, and the patient susceptible. The fact that gonococcal metastasis is so rare in gonorrhœa appears to support Lofaro's contention.

The metastasis has been recorded by Resnikow [19] as early as the fourth day after exposure to infection.

The earliest case of joint infection we have seen occurred five days after infection in a child suffering from ophthalmia.

The opinion has been expressed that the arthritis may be a toxic manifestation. While it is possible that some of the arthralgias are toxic in origin, there is ample evidence that, in the more severe cases which lead to a serous or serofibrinous exudate, the joint tissues are invaded by the gonococcus. Nasse and Rindfleisch,[20] in 1897, obtained pure cultures of gonococci from the joint fluid in 19 out of 30 cases, and Baur,[21] in 1901, in 19 out of 27 cases. Thomson,[22] in 1923, found the organism in the joint fluid in ten cases. These workers emphasise the importance of a good technique and special media. Thomson states that the culture requires to be incubated for at least ten days, as, in his experience, the growth of

gonococcus did not show up until the seventh day in one case and the tenth day in another. McDonagh [23] found the aspirated effusion from the joint to be sterile in nine cases. It is possible that, after the first five or six days, the organisms may localise themselves in the synovial membrane, the cartilages, or the epiphyses, and that the intra-articular exudate which results from this localised infection is in the nature of a sterile serous exudate.

Site of Primary Focus.—In the male it is generally accepted that the prostate gland and the seminal vesicles are the common foci from which the infection spreads to the blood stream. It is difficult to prove this in acute cases because the whole urethral tract is the site of an acute infection in addition to the prostate and vesicles. In chronic cases, however, and in acute exacerbations occurring in the course of a chronic case, there is ample evidence that these anatomical areas are the common reservoir for latent gonococci.

Michel, [24] in examining thirty-three cases of arthritis, found in twelve of them that there was involvement of the anterior urethra only. In our series the posterior urethra was involved in 100 per cent. of the cases, and we were able to find evidence of prostatitis or vesiculitis in over 90 per cent. of these cases.

In adult female patients, the urethra and cervix were involved in close on 80 per cent. of the cases of arthritis. The Bartholinian gland was infected in about 40 per cent. of the cases.

We have referred to arthritis as a complication of ophthalmia neonatorum. In 1899, Clement Lucas [25] published records of three cases which he had referred to in 1885 and in 1890. He states that Deutschmann isolated the organism in fluid aspirated from an inflamed joint complicating a case of purulent ophthalmia. Since then cases have been reported by Johnstone, [26] Fischer, [27] Pritzi, [28] Herzfeld, [29] and others.

Two cases occurred in our series as a complication of ophthalmia.

In a series of 200 cases of vulvo-vaginitis in young girls, there has been no case of arthritis. This is rather at variance with the observation of McDonagh, who states that arthritis is not an uncommon complication of vulvo-vaginitis. In a series of cases reported in the *American*

Journal of Diseases of Children (Vol. III., 1927), rectal gonorrhœa in children is stated to be a common cause of metastatic arthritis, fifty-three out of sixty-seven cases showing joint complications. In our experience rectal gonorrhœa is not common in children suffering from vulvo-vaginitis.

Time of Onset of Arthritis after Primary Infection.—The earliest adult case which we have seen occurred five days after the urethral infection; in general, the joint manifestations occur within the first four to five weeks in 80 per cent. of the cases. In complicated and chronic cases the onset of the arthritis may be later, and cases of arthritis have been recorded as occurring fifteen to twenty years after the onset of gonorrhœa. In these late cases the metastatic infection of the joint may follow the passage of an instrument for the treatment of stricture, or the lighting up of some latent focus in the cervix or in the Fallopian tubes after a pelvic operation. These late cases are usually monarticular, or at the most involve one or two joints only.

Involvement of Joints.—The disease may be monarticular or polyarticular, the percentage in our cases being 15 per cent. monarticular and 85 per cent. polyarticular. An arthritis occurring late in the course of the disease tends to be monarticular. The large joints are involved with greater frequency than the small ones and the knee is affected most frequently. The order of frequency in our series was as follows :—

Knee	64·2 per cent.
Ankle	36·8 ,,
Metatarso-phalangeal	34·7 ,,
Shoulder	23·1 ,,
Wrist	14·1 ,,
Metacarpo-phalangeal	13·6 ,,
Elbow	11·5 ,,
Hip	4·2 ,,
Intervertebral	3·1 ,,
Temporo-mandibular	2·1 ,,

The statistics of Northrup,[30] Finger, and Bennecke show that the joints were involved in the following frequency in a series comprising 704 cases :—

	Northrup.	Finger.	Bennecke.	Total.
Knee	91	136	31	258
Ankle	57	59	9	125
Wrist	27	43	6	76
Elbow	18	25	10	53
Shoulder	16	24	4	44
Hip	16	18	8	42
Temporo-maxillary	2	14	—	16
Small joints of foot	40	—	6	46
Heel and toes	21	—	—	21
Small joints of hand	11	35	4	50
Sterno-clavicular	3	—	—	3
Other articulations	—	21	—	21

Lumb's [31] figures in 464 cases are as follows :—

Knee	213	45·9 per cent.
Ankle	106	22·8 ,,
Wrist	30	6·4 ,,
Shoulder	29	6·2 ,,
Feet	27	5·8 ,,
Hip	19	4·09 ,,
Hand	17	3·6 ,,
Elbow	15	3·2 ,,
Temporo-maxillary	4	·86 ,,
Sterno-clavicular	2	·43 ,,
Intervertebral	2	·43 ,,

The joints of the right side of the body appear to be more frequently involved than those on the left, and the wrist joint is attacked more frequently in women than in men. In female patients arthritis is more common in association with infections during pregnancy and the puerperium.

Pathology and Clinical Types.—Acute cases may be subdivided into four types :—

(1) Arthralgia, in which one or more joints may be painful but there are no gross physical signs of disease.

(2) An acute infection of one or more joints, usually the larger ones, in which the inflammatory process is confined largely to the synovial membrane, which becomes hyperæmic ; there is a considerable effusion of fluid in the joint and fluctuation can be detected.

In some of these cases, apart from a slight œdema, the capsule and the periarticular structures are not involved.

In others the capsule and the periarticular structures are thickened and very œdematous, due to an inflammatory exudate into them.

(3) An acute infection in which, in addition to the synovial membrane, the cartilaginous surfaces become eroded and small flakes of necrosed articular cartilage become detached or are loosely attached to the ulcerated or eroded area.

The effusion in this type of joint infection is more in the nature of a serofibrinous exudate, and is less in amount than in the purely synovial type.

The capsule and the periarticular tissues are nearly always attacked, and are the site of fibroplastic changes following on the serofibrinous exudate.

In some of these cases, especially in the smaller joints, the swelling is almost entirely periarticular and involves the capsule, the bursæ, and the tendon sheaths surrounding the joint. If the inflammation is unchecked, the serofibrinous exudate leads to the formation of intra- and periarticular adhesions and subsequent deformity.

In a few cases, in the larger joints, there may be considerable destruction of the articular surfaces, the ligaments give way, and subluxation of the joint follows with marked deformity.

(4) An acute infection involving the synovial membrane and the articular surfaces with marked hyperæmia of all the vascular structures. The intra-articular exudate becomes purulent, and there is marked ulceration and erosion of all the cartilaginous surfaces. This type occurs in the large joints, and periarticular changes are often present. It is rarely met with. It is often stated that purulent cases result from a mixed infection, but the bacteriological studies of Young [32] have proved conclusively that in many cases the gonococcus is in pure culture and is alone responsible for the pyarthrosis.

Subacute and chronic cases may be subdivided into two main types :—

(1) A synovial type, involving especially the knee joint. The synovial membrane is thickened, and there is a moderate degree of effusion into the joint. If the amount of fluid is large and untreated it may produce a laxity of the ligaments. The periarticular structures are not involved to any great extent.

This type may evolve from the untreated acute

synovitis, or the joint condition may be subacute from the commencement if the metastatic infection is not a virulent one.

(2) A mixed type, involving both the synovial membrane and the articular surfaces, and frequently polyarticular in the smaller joints, in which the serofibrinous exudate is always fibroplastic, and leads to adhesions and deformity. Proliferative changes are more evident than destructive ones, and the periarticular tissues are involved in the fibroplastic process in almost every case.

It may result from an untreated acute case; in others the condition is subacute from the onset, with just a slight effusion of plastic lymph into the joint and a considerable amount of periarticular swelling.

Symptoms and Signs.—The variability of the symptoms is a distinguishing feature. It depends on the virulence of the infecting agent when it reaches the joint, and on the resistance of the tissues of the host. The stage of exudation is rarely reached in mild cases, and the inflammation manifests itself clinically by the onset of arthralgic pain, which flits from joint to joint without giving rise to any physical signs of inflammation. This pain is usually of short duration, but may last for days. In some cases, and especially if the primary focus is untreated, it merges into a definite acute arthritis involving one or more joints. Pain is then a marked feature, and the pain is persistent and is aggravated by movement.

If the effusion is chiefly synovial, the swelling increases rapidly, and involvement of one joint may be followed by another. As the joints swell, the pain becomes more intense; the skin over the surface is red and œdematous. The presence of fluid can readily be detected in the joint, and the bursæ, in relation to the joint, are often distended with fluid. There is frequently an inflammatory tenderness along the tendon sheaths and in the muscles acting on the joint.

If the infection is involving all the joint structures and the periarticular tissues, there is not so much swelling in the joint cavity, because the effusion is more of a serofibrinous character, and is less in quantity. The tissues surrounding the joint are œdematous and swollen, and feel thickened. The joint and the regions over the tendon sheaths are very tender to touch; they feel hot,

but the skin surface is not so red and the process does not advance so rapidly as in the synovial type; tenosynovitis is common. Movement of the joint aggravates the pain, and the muscle tissues are often the site of an inflammatory myositis. In both cases the temperature reaction varies from 101° to 103° F.

In the few cases in which the infection proceeds to suppuration, the temperature rises still higher. Pain is more severe because of the destruction of the cartilaginous surfaces. Starting pains, especially at night, and sweating, which is more characteristic of acute rheumatism, become prominent clinical features. Fluctuation can be detected easily. The general health is more seriously affected, and the patient looks ill.

When the small joints of the hand and foot are affected, pain, heat and redness are as prominent as in the larger joints, but the swelling is not so pronounced. The tendon sheaths and periarticular tissues are invariably involved. Suppuration is extremely rare in small joints.

In subacute and chronic cases the swelling is often in the nature of a hydrops. Swelling is the chief clinical sign in hydrops. Movement is not limited except by the amount of fluid in the joint, and the pain is slight and is only present on movement. The common site for hydrops is the knee joint. If the effusion is untreated it may distend the joint and lead to laxity of the ligaments. It is very apt to be recurrent if the original focus of infection is not eradicated.

In subacute and chronic gonococcal osteoarthritis the smaller joints are attacked more commonly, although the larger joints are not immune. There is always a considerable amount of periarticular swelling and œdema, but little joint exudate. The muscles acting in the joint show marked wasting, which makes the fusiform swelling of the joint more apparent. In the subacute stages these joints are somewhat tender, but in chronic cases pain is only present if an attempt is made to move the joint. In many of the untreated cases there is marked limitation of movement, due to adhesions set up by the serofibrinous exudate, and in some cases the adhesions give the impression that the joint is ankylosed.

Diagnosis.—There is no great difficulty in the diagnosis of acute gonococcal arthritis in the male if the clinician

will remember to make tactful enquiries regarding urethral discharge, and look carefully for it. In some cases, however, with the onset of arthritis the signs of urethral disease may lessen, but in all the urine remains turbid, and examination per rectum will often reveal some enlargement of the prostate and of the vesiculæ seminales in such cases. Gentle massage of these organs enables us to express fluid, in which the gonococcus may be demonstrated. It is more difficult to be accurate in the diagnosis of acute cases when they follow on a slight exacerbation of a chronic focus of gonococcal infection in the vesicles, or after the passage of an instrument for stricture.

In most acute cases the history, the discharge, and the presence of gonococci in it make the diagnosis certain, except when a sufferer from gonorrhœa develops an acute arthritis from some other cause, such as tuberculosis.

If there is no obvious focus of gonococcal infection, it is always important to exclude this type of infection by repeated examinations, when an acute, subacute or chronic affection of a joint is painful, persistent, and associated with periarticular changes. If the organism can be isolated from the joint fluid the diagnosis is definite, but failure to find the gonococcus in the fluid does not preclude its presence.

It is important in acute cases to be able to differentiate between acute rheumatism and a gonococcal arthritis.

The following are the main distinctions :—

	Acute Rheumatism	*Gonococcal Arthritis*
1.	No evidence of genito-urinary disease.	Often definite urogenital symptoms and signs.
2.	Marked temperature reaction and more prolonged constitutional upset and prostration.	Very moderate temperature reaction, and constitutional upset slight, except in purulent cases.
3.	Sweating very profuse, with acid odour.	Very little sweating except in purulent cases.
4	Pain intense and aggravated by the slightest touch.	Pain less intense.
5.	Many joints involved, but as pain leaves one it flits to another, and the first affected appears to be free from discomfort.	May be limited to one joint, and usually one or two joints only, and pain does not leave a joint rapidly and pass to another.
6.	Tendon sheaths and periarticular tissues rarely involved.	Tendon sheaths very frequently the site of disease, and also periarticular tissues.

7. More common in women.	Less frequent in women.
8. Often some cardiac complication, such as endocarditis or pericarditis, and an active focus of infection in the tonsil.	Cardiac complications very rare, and no acute condition in the tonsil.
9. Symptoms and temperature react extremely well to the administration of salicylates.	Salicylates have little effect on the pain, the swelling, or the temperature.
10. Complement-fixation test of blood negative.	Complement fixation for gonorrhœa test always positive.
11. Temporo-mandibular joint rarely involved.	May be involved.

Acute gonococcal arthritis must, in addition, be differentiated from arthritis following on pneumonia, dysentery, cerebro-spinal, typhoid, or scarlet fever, acute tonsilitis, and tuberculosis.

An acute tuberculous arthritis is slower in its onset, it is rarely polyarticular, the pain is not so severe at first, there is often epiphyseal involvement, and X-ray examination will reveal a definite lesion of the bone, which is not common in gonorrhœa.

In pneumococcal cases the joint fluid almost always shows the presence of pneumococci. In other cases of pyogenic arthritis the typical signs of the active disease, such as scarlet and typhoid fever, etc., are of the greatest help in accurate diagnosis.

Subacute and Chronic Cases of Gonococcal Arthritis

Subacute and chronic cases of gonococcal arthritis are very difficult to diagnose from those due to other bacterial infections, such as *Bacillus coli*, various streptococci and pneumococci, *B. tuberculosis*, *B. Dysenteriæ*, and the *Streptococcus rheumaticus*. The various forms of chronic infective, or " rheumatoid," arthritis, osteoarthritis, and the early stages of the arthropathies or trophic disturbances, as in tabes dorsalis or syringomyelia, may stimulate a chronic gonococcal joint.

A subacute joint condition which is persistent and shows periarticular changes should always prompt us to exclude a gonococcal infection. This necessitates an examination for urethral discharge and of the urine; bacteriological tests of any secretion or of the centrifuged deposit of the urine should follow, and, in addition, rectal palpation and massage of the prostate and vesicles to

express their contents for examination by direct film or by culture. Even if gonococci are not demonstrated in any of the examinations, the presence of pus cells in the prostatic or seminal secretion is suspicious. It should lead us to give the patient an injection of an emulsion containing 200 to 400 millions of dead gonococci to stir up any latent focus of disease ; the clinical and bacteriological tests are repeated 36 to 48 hours subsequent to this injection.

Similarly, in a female, suffering from chronic arthritis, it is important to examine the urethra, the Bartholinian ducts and glands, the endocervix, the Fallopian tubes, and the pelvic cellular tissues in searching for a focus of infection. Direct films and cultural tests are carried out after administering an injection of polyvalent vaccine, or after inserting a plug of gauze soaked in glycerine into the endocervix. The best time to examine the female for signs of latent gonorrhœa is post-menstrual.

In both sexes a positive result in the gonococcal complement-fixation test of the blood may help to establish the ætiology of the joint affection. If any suspicious sign of infection is found in either sex, the reaction to treatment is often of considerable assistance in diagnosis.

In distinction from chronic tuberculous joints, gonococcal cases are more often polyarticular, with the exception of a hydrops. The X-ray appearances are different from those of tuberculosis. The fasciæ and aponeurosis are more often affected in gonococcal affections, and a raised temperature in the joint is more common in tuberculosis. Wasting of the muscles acting on the joint is stated to be more common in tuberculosis, but this is also a prominent feature of chronic gonococcal arthritis.

In differentiating from other forms of chronic infective arthritis, the X-ray appearances in the cartilage and bone are helpful, especially in excluding an early rheumatoid arthritis. A history of recurrent attacks of iritis in a patient suffering from arthritis strongly suggests a gonococcal ætiology.

X-ray Appearances in Gonococcal Arthritis

In acute joint involvement this is of little assistance except in differentiating from acute tuberculous disease.

If the intra-articular exudate is marked there is an apparent increase in the joint space. If the infection is involving both synovial and articular surfaces, the joint space may be decreased by the absorption of cartilage. These appearances, however, may result in any acute pyogenic arthritis, although in gonococcal cases they occur less rapidly, and are rarely so extensive except when the arthritis sets in during pregnancy and the puerperium.

The radiographic appearances in chronic gonococcal arthritis simulate those of any chronic infective arthritis. In tuberculosis there is often definite evidence of osseous change, especially in the region of the diaphysis, and the changes are destructive, and not proliferative and reparative, as in gonorrhœa. In rheumatoid arthritis there is distinct lipping of the articular surfaces, and although the joint space is diminished as in tuberculosis, the definition is usually better in non-tuberculous arthritis. When the activity of a tuberculous joint has ceased the definition becomes more distinct, but the articular surfaces have a worm-eaten appearance.

Complement-Fixation Test in Gonococcal Arthritis

In acute gonococcal arthritis the test gives a positive reaction in a large number of the cases (75 per cent.), if it is carried out later than ten days after the infection. In subacute and chronic cases in which the arthritis is generally later in appearing, the number of positive results is larger still, and is close on 80 per cent.

A negative complement-fixation test does not exclude gonorrhœa as the cause of the joint infection ; a positive test is strong confirmatory evidence of its ætiology. The test is of considerable value in obscure cases of joint infection, in which the clinical findings in the genito-urinary tract are suggestive, but in which repeated bacteriological tests have failed to show the gonococcus. If the fixation test, and at the same time cultural and bacteriological tests, are negative, it is the strongest possible evidence that the joint condition is not due to gonorrhœa.

Thomson [33] found the test positive in twenty successive cases of acute gonococcal arthritis, varying in duration from one to thirty days ; in thirty-three chronic cases, of one to twelve months' duration or longer, 94 per cent.

gave positive reactions. Wilson, Forbes and Schwartz [34] found positive results in 47 per cent. of their acute cases, in 73 per cent. of chronic cases, and in 60 per cent. of doubtful cases.

Horder,[35] in reviewing the foregoing work, lays emphasis on the value of the test in chronic cases, because in these " we are denied the advantages of direct bacteriological proof, the smaller percentage of positive results in acute and subacute cases is not such a material loss as might at first be thought."

Besançon, Weil and Rubinstein [36] found 87·5 per cent. of positive results. Fourteen cases of arthritis of non-gonococcal origin all gave negative results. There is, in their opinion, no other type of arthritis which gives a definite positive result, and hence the test, when positive, is of considerable assistance in cases of obscure ætiology.

In cases of undoubted gonorrhœal arthritis, Thomas and Ivy [37] state that the test is simpler than a bacteriological examination, and gives more positive results. In acute cases 100 per cent. positives are found, and there are no false positives in arthritis due to other conditions. Osmond,[38] in a series of 1,000 tests, comprising 300 men and 700 women, considers that this test is at least as valuable as the Wassermann test in syphilis. In undoubted gonorrhœa he finds a high percentage of positives (86·5 per cent.), while false positives are extremely rare.

Thomson's results are as follows :—

Acute arthritis (1 to 30 days)	. 100 per cent.	positive.
Chronic arthritis (1 to 12 months)	94 ,,	,,
Chronic rheumatism with no evidence of gonorrhœa	. . 100 ,,	negative.

Osmond stresses the value of the test as confirmatory in diagnosis, and Thomson considers it a powerful diagnostic agent.

Cuti-Reaction.—An intradermal skin test on the principle of the Von Pirquet Test has been tried by Brewster [39] in 1,000 cases ot gonorrhœa, including over 100 cases of arthritis. The test was positive in over 80 per cent. of cases of gonorrhœa, and there were only 0·6 per cent. of false positives. In gonococcal arthritis positive reactions were obtained in 98 per cent. of the cases.

Prognosis.—The prognosis in the first three groups of gonococcal arthritis, (*a*) arthralgia, (*b*) acute and subacute

synovitis, and (*c*) acute and subacute synovitis and arthritis, is invariably good, even if there is involvement of the periarticular structures, if treatment of the original focus of infection, and of the joint, is given on correct lines. In the fourth group, acute arthritis with suppuration, surgical interference is often required, and there may be considerable loss of function. Cases of subacute or chronic hydrops react moderately well to treatment on the same lines as the first three groups, but recovery is always slow, and the joint condition is apt to recur. Cases of chronic osteoarthritis, in which adhesions have been allowed to develop, are very difficult to treat effectively. Although the joint condition can be made stationary, there is almost always some limitation of movement and loss of function.

Luys [40] is rather pessimistic in stating that "acute arthritis seldom ends by resolution. Its usual termination is ankylosis." We have on record many cases which have cleared up completely without any evidence of ankylosis, while in this series of cases there was only one death, a case of gonococcal septicæmia complicated by keratodermia and an intercurrent pneumonia.

In the course of our work we have investigated numerous cases of chronic infective arthritis because of these patients having given a history of previous gonococcal infection. We have been impressed by the fact that the damage which may accrue to a joint from a previous gonococcal infection which has not been cured, predisposes to the onset of rheumatoid arthritis in the joint. In summing up prognosis, we can state that if radiographic examination of the acutely infected joint shows no destruction of the articular surfaces, the prognosis is always good. If there are changes in the articular surfaces, the prognosis for function must be guarded, although in many cases the patient can be assured of having a useful joint with very little limitation of movement.

Treatment.—Whether the arthritis is due to the absorption of toxins from the genital and urinary tract, as in arthralgia, and their transference to a joint, or to the spread of gonococci by the blood or lymph stream to the joints, as in more severe cases, the rational treatment, or an essential part of it at least, must be to cut off the source of supply of toxins or organisms by *treating the original*

focus of infection in the genito-urinary canal and in the zones to which it may extend locally. Plisson [41] goes so far as to state that the best preventative of gonococcal arthritis is the early and thorough treatment of the primary infection. We are in complete agreement with this statement, and it is noteworthy that, in 99 per cent. of all our cases, a joint complication had developed before the patient was treated or after ceasing treatment before being cured. In only three cases did an arthritis develop in a case while under active treatment. Further, *the infected joint must be treated locally*, to relieve pain, to prevent the formation of adhesions, and to restore the limb, and especially the joint, to its normal functional activity. In addition, in most of the joint cases we are dealing, as Horder [42] states, with a condition of pyæmia, and therefore *specific treatment should be applied through the blood stream* to influence the blood-borne infection. Lastly, *the general condition of the patient must be treated* with a view to raising the resistance to the infection.

There is great diversity of opinion as to the relative value of these methods, and still further diversity as to the best methods of applying these four methods of treatment :—

(*a*) General.
(*b*) To the original focus of infection.
(*c*) To the infected joint.
(*d*) Through the blood stream for the pyæmia or septicæmia.

(*a*) *The General Condition of the Patient.*—The most important indication in acute arthritis is rest. At the same time, the elimination of the toxins must be improved by the administration of diuretics, by tepid sponging to induce diaphoresis, by aperients, and by hot hip baths. Light nourishing diet with abundance of bland fluids between meals is necessary to keep up nutrition. In acute infections of the female, Liquor Sedans ʒi, and Tr. belladonna minim v to x, is given thrice daily during each menstrual period to prevent a spread of the infection to the upper genital tissues.

Many drugs have been tried for the relief of the arthritic pain. It is generally agreed that salicylates have little effect on the pain, although Bodenstab [43] strongly advocates their use and that of amidopyrin. In many of

our cases, novalgin was effective in giving relief from pain. In acute prostatitis and vesiculitis, suppositories of atropine and morphine are often indicated. In more chronic cases, iodides, syrup of iodide of iron, French codex iodine, and general tonics help to improve the general condition.

(*b*) *The Original Focus of Infection.*—The earlier and the more efficiently this is treated, the less likely is the development of any metastatic infection. If the infection is confined to the anterior urethra, arthritis is rare, and the aim in all cases of male infection is to confine it to these limits. In female cases, if the infection, as a result of early treatment, is confined to the urethra and the cervix, arthritis will be less prevalent.

In very acute cases of arthritis the treatment of the urethra may be difficult. Irrigation of the urethra and bladder with an antiseptic, such as potassium permanganate, is the best method in both sexes. Many other efficient antiseptics are available. If irrigation cannot be carried out, Styli of Citragan may be introduced into the urethra, as advocated by Kissmeyer.[44]

In female patients the Bartholinian gland and the cervix require local antiseptic treatment. In the former, the injection of electrargol into the infected gland or duct, or complete excision of the gland, give good results; in the latter, antiseptics, of which there is a large selection, should be applied to the cervix with dressed probes.

In cases of ophthalmia neonatorum, of vulvo-vaginitis, and of proctitis, local antiseptic treatment is always required.

When the infection in the genito-urinary canal is subacute, other methods of eliminating the disease require to be brought into use. The aim of these methods is the drainage of the urinary canal and the associated zones of infection. In men, the focus of infection from which an arthritis emanates is often situated in the prostate gland and seminal vesicles. It is thus important to secure drainage from these areas by massage at intervals of three to five days. Massage of these tissues per rectum is of paramount importance in all cases of arthritis, and should be practised as soon as the urethral infection has become subacute. It lessens the pyæmic infection and helps to eradicate the disease; if these areas are made free from infection, recurrent attacks of arthritis do not

readily occur. At the same time, other areas of infection, such as Littré's glands, are treated by the careful application of such measures as suction and dilatation. If, in the revolving stages of gonorrhœa, the infected areas in the prostate and vesicles are slow in clearing up, the passage of a large posterior sound or instillations of silver nitrate, 1 to 2 per cent., or of mercurochrome, 1 to 5 per cent., into the posterior urethra or into the common ejaculatory duct, will often promote drainage and expedite recovery. In the subacute stages of infection in the female, instrumentation may also be required, such as suction of the urethra or cervix by Mills' negative pressure catheters. A course of hot douching at a temperature of 104° to 112° F., and the insertion of tampons of 20 per cent. ichthyol in glycerine, may be required in subacute and chronic infections of the Fallopian tubes, or the pelvic cellular tissues. A chronic infected Bartholinian gland should be excised. In gross disease of the Fallopian tubes it may be necessary to remove the tubes after the acute condition has subsided.

Operative Measures Directed to Sterilising the Vesicles

Vesicles.—We have drawn attention to the frequency of infection of the seminal vesicles in cases of arthritis in men. This has led to the practice of applying antiseptic treatment direct to the infected vesicle through the vas deferens in both acute and chronic cases. Vasotomy and subsequent lavage of the vesicle with 20 c.c. of 5 per cent. collargol was introduced by Belfield [45] in 1905, and has been practised to a great extent chiefly by American workers. In 1920, Belfield [46] published a revised technique of his operation. He bases the justification of this method of treatment on the physiology and histology of the seminal vesicles, and believes that it is the most efficient method of sterilising the vesicles. Thomas [47] advocates vasopuncture once only, and injection of 5 per cent. collargol or 20 per cent. silver proteose as less likely to lead to permanent injury to the vas deferens.

Kidd,[48] in 1923, published the details of his operation of vasostomy, which differs slightly from that of Belfield. He recommends the temporary fixation of the vas to the skin surface for about seven days, to enable at least three

instillations of 10 c.c. of 5 per cent. collosol silver to be introduced in a period of one week. Wolbarst [49] recommends argyrol, 5 per cent., and also chlorazene solution, 1 in 200, as an instillation, and more recently, in 1928, Belfield and Rolnick [50] have suggested for instillation a solution of aristol in cod liver oil (10 grms. of the former in 30 c.c. of the latter, or goose oil).

These authors stress the excellent effect of this measure not only on the infected vesicle, but on the concomitant arthritis. Wolbarst considers vasostomy the most dependable single measure for the relief of arthritis, and Lowsley [51] states that it is an essential part of the treatment in association with autogenous vaccines. Kidd states that all his cases were cured by vasostomy in three weeks, and that the joint troubles disappeared rapidly. Wolbarst goes so far as to state that no case of arthritis can be cured without this operation, an expression of opinion with which we cannot agree. In our experience, vasotomy and vasostomy have not resulted in the spectacular cures claimed by those who advocate this operation ; we have seen cases of arthritis on whom the operation was performed by others without any appreciable improvement and certainly without cure.

In the acute and subacute cases in our series, practically 98 per cent. were cured without any operative measures, and the affected joints were restored to good function. In chronic cases which are resistant to all other forms of treatment there may be a field for vasostomy, if the vas is still patent, and if the vesicle is still infected. In our opinion, those who advocate operation on the vesicle as the main measure in the treatment of arthritis are apt to forget that in the greater number of these cases, and certainly in acute cases, the gonococcal infection involves the prostate and possibly other zones of infection on which vasostomy and instillation of antiseptics has no effect.

Other operations which have been practised are vesiculotomy and vesiculectomy. Drainage and excision of the vesicles were introduced in 1901 by Fuller. Thomas [52] recommends vesiculotomy or drainage in cases of suppuration of the vesicle and in cases of perivesiculitis ; on the other hand, L. L. Michel [53] states that he has not obtained favourable results from the operation, and A. H. Freiberg [54] is emphatic that operation on the vesicles alone cannot possibly cure an infected joint. Thomas recom-

mends vesiculectomy in cases of perivesiculitis. Cunningham,[55] and also Greenberg,[56] claimed good results from this operation. In chronic cases, Cunningham considers that vesiculectomy gives striking results in the relief of pain, and in the reduction of articular, and especially of periarticular, swelling.

In our experience there are few, if any, cases of acute arthritis in which such a severe and difficult operation is necessary. In chronic cases the operation cannot be expected to clear up destructive lesions in the joint and cartilage. These operations should be reserved for cases in which every other form of therapy has been tried and found ineffective.

Stellwagon and McCahey [57] inject 3 c.c. of Pregl's solution directly into the vesicle through the rectal wall. This is an aqueous isotonic solution of the sodium salt of hydriodic acid and iodic acid with metallic iodine (0·04 per cent.); after three to four injections into the vesicle these authors claim that in fourteen cases of acute vesiculitis the arthritis was cured. This operation may favourably influence the acute vesiculitis, but there is always a great risk of introducing a secondary infection into the punctured vesicle and a gonococcal infection to the rectum. Further, it is not rational to expect that a focus of infection in the joint will automatically subside as a result of antiseptic treatment applied only to the contents of the vesicle.

Townsend [58] has reported favourable results from the intraprostatic injection of what he terms "a normal phenol serum," in prostatitis and vesiculitis. This method was tried in Franks' clinic in Berlin and discarded as valueless.

In three of our subacute cases vasostomy was performed, and instillations of collargol were made into the vesicle, but failed to effect a cure of the arthritis or the gonorrhœa. We have also had under our care cases operated on by others with moderate results.

(*c*) *Methods of Treatment of the Affected Joint.*—The aim of local treatment to the joint is to relieve pain and bring about resolution of the synovial or periarticular swelling. Rest and immobilisation of the affected joint help to relieve pain; a light poroplastic splint or sandbags will immobilise the lower limb; a sling is usually effective in the case of the upper limb. Sedative applica-

tions should be applied to the joint, such as lead and opium, 20 per cent. ichthyol in glycerine, glycerine and belladonna, antiphlogistine, or similar applications.

In subacute and chronic cases rest is not required to the same extent, and local applications should be more stimulating. An ointment incorporating iodine, thymol and ichthyol, or one containing gr. 40 of acid salicylic in unguentum capsici, 1 oz., is a very effective counter-irritant to the infected joint. Iodex or tincture of iodine may be used, although the latter is apt to injure the skin surface if applied continuously.

In the declining stages of an acute infection, and in chronic cases, the application of Ungt. Hydrarg Co. (Scott's dressing) is a mild stimulant, and assists vascularisation. Bier's passive hyperæmia can be applied in all acute and chronic cases, and is very valuable. It does not interfere with other local treatment. It relieves pain and assists in the absorption of inflammatory products. Baetzner [59] strongly advocates Bier's engorgement treatment daily for twenty-two hours with the limb elevated. He emphasises the need for keeping the limb red and hot, and not pale. Hot-air baths, ionisation, and other physio-therapeutic methods are helpful in relieving pain, but do not give any greater relief from pain than can be attained by simpler methods.

In dealing with all acute cases, with the exception possibly of a pyarthrosis, and in subacute and chronic cases, the early institution of passive and voluntary movement and massage of the affected joint, and of the muscles acting on it, are measures of paramount importance if the best functional results are to be obtained. Movement and massage must be practised as soon as the acute pain is relieved. This is the most effective way of avoiding permanent joint disability, and does so in our experience, except in those cases which on X-ray examination show signs of cartilaginous or osseous damage. It prevents adhesions being formed from the serofibrinous exudate, and must always be an integral part of any method of treatment. In the literature on this aspect of treatment, Collins [60] is almost the only advocate of more complete and longer immobilisation of the joint. He applies a plaster case to the joint for at least two weeks. It is then removed to permit of massage and passive movement, and is reapplied for a further period of two

weeks. This method will certainly eliminate pain, but undoubtedly the risk of ankylosis is too great for it to be recommended.

Diathermy.—Cumberbatch [61] introduced this method of treatment of arthritis in 1913, and with Robinson he has reported very favourable results in gonococcal arthritis. They advise the application of the "high frequency" alternating electric current to the infected prostate and seminal vesicles at the same time. This current produces deep-seated heat without leading to any chemical change in the tissues, or to nerve or muscle stimulation. It is thus more valuable than the continuous electric current. Further, the heat to which the tissues can be raised, 112° to 114° F., is stated to be lethal for gonococci. Certainly, *in vitro*, gonococci are either devitalised or destroyed by a temperature of 102° to 105° F. Pelouze [62] is doubtful if the heat produced by diathermy to 112° F. will destroy the gonococcus *in vivo*.

Cumberbatch and Robinson's methods, published in 1923, appeared to be a very definite advance in the therapy of gonococcal arthritis. In this country, very few further reports have been published in confirmation of their claims except by these same workers. Van Putte [63] reported good results in a few cases of chronic gonorrhœa. Acute cases, in his experience, did not respond well to the treatment. Kovacs [64] found diathermy most effective in subacute and chronic cases.

In our experience over a period of six years, diathermy, when applied to the joints only, is not a cure. Diathermy to the focus of infection alone is no more successful. Diathermy applied to the joints, and also to the focus of infection in the prostate and vesicles, or in the cervix, is helpful. It relieves pain, reduces the swelling, and assists in vascularising the part. The temperature to which the tissues are raised may devitalise the gonococcus, but does not always eradicate it from the prostate and vesicles. Cell metabolism may be stimulated, and the tissue resistance to the gonococcus may be increased. In estimating its value as compared with other methods which are more within the compass of the work of most practitioners, we are not convinced that it is very much superior to the local application of heat to the joint, by antiphlogistine, and to hot rectal irrigations in acute

prostatic and vesicular infection. In subacute and chronic cases it cannot replace massage of the prostate and vesicles ; it does not enable us to dispense with voluntary and passive movements in restoring the joints to full function. In addition, it rarely exercises any favourable effect on the infection of the urethral canal, and unless other local treatment is administered at the same time there is always the definite possibility of a recurrence of the infection in the prostate and vesicles, or even in the joints.

Diathermy is a useful adjuvant form of treatment, but by itself it is not a complete cure of either the prostatic and vesicular infection or the joint infection. We cannot agree with the claim of Cumberbatch that " the results of treatment by diathermy are far superior to those obtained by any other method."

Coyon and Gagey [65] treated five cases of arthritis by *radium* to the joint. They claimed almost immediate relief from pain, and very rapid improvement in acute cases. It is not, in their experience, efficacious after ankylosis has occurred. They recommend early mobilisation at the same time. We have had no experience of this method.

Operative Treatment of Gonococcal Arthritis

In acute cases, aspiration of the affected joint, aspiration followed by irrigation with antiseptics, and arthrotomy followed by joint irrigation and drainage, have all been advocated and practised. In 1899, O'Conor [66] reported good results in ten cases treated by arthrotomy, irrigation and drainage. Klose [67] also favours this method in selected cases, and especially if signs of subluxation are present, or if the joint condition does not show signs of improvement with three weeks conservative treatment. Harrison [68] and others state that aspiration of the acutely inflamed joint gives good results in the relief of pain. Knauer [69] reports two cases of joints in which cure was attained by aspiration only. Barzy [70] discusses the merits of surgical treatment, suture without drainage and early mobilisation, and the advantages of intramuscular injections of serum. The latter method he considers more satisfactory, but in some articulations, such as the wrist, and especially if the tendon sheaths are

involved, it may fail. In cases in which serum treatment fails he advises emptying the joint of its contents. Joint puncture, together with lavage and injections of 1 in 5,000 Vuzin solution, is favoured by Mobitz,[71] who obtained excellent results in the ten cases in which he used this method. Dufour, Thiers, and Alexewsky [72] claim most favourable results from aspiration of the infected joint, and reinjection of 10 to 20 c.c. of the aspirated fluid into the subcutaneous tissues of the thigh. It is immaterial, they state, whether the fluid is serous or purulent, and they claim that this method influences the original focus of infection favourably. Ballenger and Elder [73] reported successful results in twenty-seven cases of gonococcal arthritis by aspirating 15 to 20 c.c. of synovial fluid and reinjecting it into the gluteal muscles at two-day intervals without any other adjuvant treatment. Churchman [74] aspirates the joint and washes it out in turn with saline solution, hydrogen peroxide, and saline solution again. He then instils a solution of 1 in 1,000 gentian violet into the joint cavity and allows it to act for five minutes. This is reaspirated from the joint and a fresh supply of 1 in 10,000 gentian violet is injected and left in the joint cavity. Walther [75] also advocates joint puncture and lavage of the cavity in acute cases. Freiberg [76] considers that the main site of the infection is the synovial membrane. He opens the joint by a small incision, flushes it out well with sterile water at a temperature of 115° F., to kill the organisms, and closes the joint without drainage. Plisson [77] also states that the best method of treating an acute joint is puncture or incision, followed by washing and closure of the joint. Antigonococcal serum diluted with physiological serum to 10 or 20 per cent. is then given by intra-articular injection. According to Klapp,[78] the best treatment is the periarticular or intra-articular injection of Rivanol in a strength of 1 in 1,000. No other antiseptic, he considers, can be compared to it in its effect on pyogenic and gonococcal arthritis. Ramond, Janet and Levy [79] tap the cavity, fill it with filtered air, and then inject 5 to 10 c.c. of iodised oil. They also advocate using a 20 per cent. solution of sodium citrate to wash out the joint after aspiration. Lavage of the joint with 2 per cent. formaldehyde and glycerine is recommended by Walther,[80] and we have found this efficient in the few cases of pyarthrosis in our series.

Mondor,[81] on the other hand, states that surgical intervention, especially incision of the joint, is uncertain as a cure, and may be followed by progressive ankylosis and joint destruction. The only thing in its favour is, he states, the immediate relief from pain and an improvement in the patient's general condition, especially if there is evidence of progressive destruction of the articular cartilages.

In our series only seven cases (1·3 per cent.) were operated on by arthrotomy and joint lavage. In these cases there was a definite purulent arthritis, in which operation was necessary to stop the destructive action on the cartilages, and for the general condition of the patient. In all the other acute cases conservative measures were employed, such as temporary immobilisation, Biers congestion, local applications of antiphlogistine, diathermy, hot-air baths, and other local measures. While these measures may not give as immediate relief from pain as arthrotomy or joint puncture, the end results are as good, if not better, than those reported after many of the operative measures previously mentioned, and the patient is not exposed to the risk of a serous synovitis becoming a purulent arthritis through the entry of other organisms into the joint structures. In chronic cases of gonococcal arthritis the pain is rarely so severe, and local applications of a stimulating character are almost always indicated. In conjunction with these measures we have used hot-air baths, diathermy, and counter-irritants to stimulate an active hyperæmia. Biers' passive congestion is indicated in chronic cases, and hastens the absorption of inflammatory exudates. Massage and active movement are of considerable value in restoring the limb to normal function. If there is marked loss of mobility and the joint is in bad position, the joint should be examined by X-ray, and if the radiographic picture justifies the procedure, it is mobilised under general anæsthesia. If there is ankylosis, arthrectomy may be required, particularly in the case of the knee joint. In all chronic cases we are convinced of the need for the co-operation of an orthopædic surgeon so that the best functional results may be obtained. In cases of hydrops, aspiration of the joint will temporarily relieve the disability, but, in our experience, the joint cavity fills up again, unless the focus of infection in the genitals is dealt with satisfactorily.

(*d*) *Specific Therapy through the Blood Stream.* (1) *Vaccines and Sera.*—The literature on this aspect of treatment is enormous, and in a review of sixty-eight articles, Thomson[82] states that sixty-six of these authors gave favourable reports, while only two failed to find any benefit from vaccines in gonococcal arthritis. The majority of observers are thus of opinion that it is a valuable therapeutic measure and a necessary part of the successful treatment of gonococcal arthritis. Different types of vaccine were administered in practically all our cases, and with excellent results. Many have advocated the use of sensitised vaccines, that is, a vaccine which has been subjected to treatment with its appropriate antiserum during its preparation. The first stage of the immunisation is thus performed *in vitro*, the vaccine is less toxic, and consequently a larger dose can be given. Cruveilhier,[83] Broughton-Alcock,[84] Haworth,[85] and Dopter and Pauron [86] all state that the administration of sensitised vaccines alleviates pain quickly, and leads to subsidence of the swelling. The initial dose which these workers used varied from 100 million gonococci by Haworth to 500 millions by Broughton-Alcock. We were able to observe several of Haworth's cases, and the results (sixteen cures in seventeen cases of acute and subacute arthritis) were extremely good. We have not used sensitised vaccines in any of the cases in this series.

In 1919 Thomson [87] published his work on the separation of gonococci from their toxins, and in 1919 Thomson and the writer [88] published the results obtained in the treatment of cases of gonorrhœa and its complications with detoxicated vaccines.

This type of vaccine makes it possible to give a much larger dose of antigen, without giving rise to a severe general or focal reaction. In this way a larger output of antibody by the patient is stimulated and is obtained. Considerable controversy was aroused by this work, and the objection was raised that antibody and antisubstances could not be produced by a non-toxic substance ; further, the removal of toxins was said to be unsound, because, when injected, they have antigenic power and tend to stimulate antitoxin production and the conditions necessary for the formation of antibody.

Without entering into these arguments, we have no

hesitation in stating that in the treatment of arthritis, detoxicated gonococcal vaccine has given consistently good results and has proved an invaluable adjuvant in the acute and subacute cases in which it has been administered in this series. We have used it in over 250 cases, either alone or in combination with an autogenous vaccine, and can state that it assists materially in the relief of pain and swelling, in cutting short the disease, and in lessening the liability to complications.

The initial dose varies with the patient's condition, and should be from 2,000 to 5,000 million gonococci; we have increased the dose progressively up to 100,000 millions in some cases. There is, in our experience, no material advantage in giving the vaccine intravenously as compared with the simpler method of intramuscular or subcutaneous injection. This is at variance with the findings of Fraser and Duncan,[89] who gave a stock polyvalent vaccine up to 2,000 million organisms intravenously; in their view, if no pyrexia followed its administration, no benefit seemed to accrue. We have compared the results obtained with ordinary polyvalent vaccines, and are satisfied that the detoxicated vaccine has many advantages, the chief of these being the more rapid effect on the original focus of infection, the quicker relief from pain, the more rapid resolution of the joint, the absence of any negative phase, and the feeling of well-being which the patient often appreciates within twenty-four hours after the injection. Sieur [90] reports that Costa, in close on 100 cases of acute gonococcal arthritis, obtained most favourable results in the relief of pain and return of function in all cases by using a polyvalent vaccine prepared with formaldehyde. Lian, Poincloux and Copelovici-Cope [91] also report most successful results and complete return of function in all their acute cases treated by vaccines. Similar results are quoted by Vallino and Macera [92] in cases of arthritis complicating vulvovaginitis. Sezary [93] considers vaccine therapy efficacious to a degree, and states that the dosage must be effective, 60,000 to 80,000 million organisms in four or five injections. He employed a lipovaccine with excellent results. Michel [94] states that while occasional brilliant results are obtained by vaccines, they were on the whole disappointing. He believes that he gets better results from them by intravenous administration, due possibly

to their action as a protein when administered by this route. He prefers non-specific proteins.

In over forty of our cases we tried the effect of "Arthrigon," a polyvalent gonococcal vaccine containing urotropin. This method was first used by Rohrbach [95] and Dorn.[96] Bruck [97] was of opinion that it was superior to any other form of vaccine, and could replace an autogenous vaccine. Bardach,[98] Martin Fischer,[99] Freund[1],[00] and Pritzi [101] all report excellent results from its use in acute arthritis. On the other hand, Hagen [102] was not impressed with the results of arthrigon and Roth, Klinger and Oppenheim [103] state that it failed to influence gonococcal arthritis favourably. Complications during treatment occurred frequently in the cases treated with arthrigon by Habermann,[104] who is not impressed with the results. In thirty-three acute cases in this series which were treated with intravenous injections of arthrigon, we noted an immediate and progressive improvement in the joint condition, and also in the primary focus of infection. Eight chronic cases did not respond so quickly, but there was a definite improvement in all of them, and in two cases of hydrops, the joint infection was cured by this method in combination with treatment of the local and focal infection. "Arthrigon," in our opinion, gives very good results in cases of acute and subacute arthritis.

Another preparation which we have used is Gono-Yatren, a suspension of polyvalent gonococci in a 3 per cent. yatren solution. Like arthrigon, it gives a specific and non-specific reaction. Four acute cases reacted favourably to Gono-Yatren, and at the same time there was a marked improvement in the genito-urinary infection. We tried the effect of gonococcal phylacogen in an earlier series of cases, and came to the same conclusions as were reported by Harrison,[105] that while in large doses a phylacogen may give rapid relief to the pain of an arthritis, this preparation does not exercise any beneficial influence on the genito-urinary infection. The results were, in our opinion, largely dependent on the amount of protein shock produced by each injection.

Serum treatment by antigonococcal serum has been employed in the treatment of gonococcal arthritis with varying results. Thomson, [103] reviewing fifty contributions on this subject, found that forty-three authors

considered it of some therapeutic value. It was first used by Torrey.[107] Rodgers and Torrey[108] reported cures or marked improvement in 78 per cent. of acute cases. Porter,[109] Louis,[110] and Steelwagen[111] obtained good results with serum treatment, and Ballenger[112] had 72 per cent. of cures in ninety cases. On the other hand, Fletcher,[113] and also Brück,[114] considered it a failure. Herbst[115] and Thomas[116] formed the opinion that it was only of value in chronic cases. Debré and Paraf[117] consider that it is necessary to bring the antiserum in contact with the organism and inject it into the infected joint cavity after aspiration. They supplement this by intramuscular or intravenous injections of the antiserum, and reported very good results in fourteen out of fifteen cases.

We have not used gonococcal antiserum in any of our cases. It has definite disadvantages as a method of treatment in that it may produce an anaphylaxis at some future date if other antisera, *e.g.*, antidiphtheritic, require to be given. In addition, general serum reactions, urticarial eruptions, and pain at the site of the injection are reported by several workers. Langeron and Bocca,[118] although admitting that it relieves the joint pain and prevents septicæmia, state that it has no influence on the urethritis.

Good results have been reported from the administration of non-specific sera by Soltau, Fenwick and Parkinson.[119] Fox[120] and also Salter[121] recommend rectal injections of 10 c.c. antistreptococcal serum.

Antimeningococcal serum is favourably reported on by Malleterre[122] and by Chiari,[123] who in reviewing the literature found thirteen cases reported cured out of sixteen treated by this method.

Auto-serotherapy by aspirating fluid from the joint and re-injecting it subcutaneously near the articulation is favourably commented on by Ramond,[124] while Ballenger and Elder[125] strongly advocate its use and do not employ any other local or general treatment. They state that the aspirated fluid must be turbid if it is to be effective, and they inject it intramuscularly into the buttock. Thomas,[126] on the other hand, states that he has never found this method of any assistance.

Protein Therapy.—The resistance of the individual to many infections can be increased by the administration

of foreign proteins, and the pyrexia so produced is possibly the chief factor in its action.

Many proteins have been used in gonococcal arthritis, such as horse serum, peptone, sterile milk, T.A.B. vaccine, and antidiphtheritic serum. Rodriguez [127] treated more than 100 cases by antidiphtheritic serum with excellent results.

In a number of our chronic cases, and in subacute cases not responding to vaccine treatment, we have found that the production of a mild protein shock by the intramuscular injection of 5 c.c. of sterile milk is often of considerable value, if interspersed between successive doses of vaccine.

In some of the most chronic cases, injections of peptone have been even more successful, as it produces a greater degree of protein shock. The initial treatment by protein shock, followed by vaccine treatment, is followed by quite favourable results in many chronic cases. We have tried the effect of repeated injections of milk in acute cases, and have not been impressed with the results.

Chemotherapeutic and Other Injections.—A very large number of these substances have been recommended in arthritis, either alone or to supplement vaccine treatment.

Intramine and contramine are advocated by McDonagh [128] in acute and chronic cases, prior to and later in conjunction with vaccines. Young [129] and others state that they have obtained good results from the intravenous administration of Mercurochrome 220. We have tried this method in three cases and agree with the observations of Brash and Bumpus,[130] who consider it is too toxic a preparation for routine administration. In addition, it did not in our cases cure the gonococcal infection. Another chemo-therapeutic substance which has been tried in infective cases of arthritis and in gonococcal arthritis is *ortho-iodoxybenzoic acid.* Young and Youmans [131] state that in hopeless cripples they obtained marked improvement in 56 per cent. of cases, some of whose joint conditions were gonococcal in origin. Millard Smith [132] states that any arthritis giving rise to pain, swelling and muscular spasm will benefit from the intravenous injection of this substance.

We used this preparation in two cases of gonococcal, and in one case of chronic infective arthritis, with no appreciable improvement. It was administered in doses

of 0·6 to 0·9 gm. dissolved in 100 c.c. of sterile saline solution, and was given very slowly. It was apt to cause venous thrombosis, and the reactions were very severe; the patients were upset to such an extent that we decided to discontinue the use of this drug. Stein and Traube [133] had a similar experience, and found it valueless in gonococcal cases. The *organic arsenical compounds* have been tried in the treatment of gonococcal arthritis, and Lamblin [134] considers that subcutaneous injections of *sulpharsenol* are easily applied and are well tolerated. The patient's general condition and the pain improve rapidly, and early mobilisation is possible. Girard and Trigher [135] are also impressed with its rapidity of action in arthritis, while Duroeux, Tant and Bernard [136] state that "*at the present moment, arsenical treatment constitutes a veritable specific for the inflammatory complications of gonorrhœa.* This treatment has very little effect on the concomitant urethritis. We have not used sulpharsenol in arthritis *per se*, but have noted that in cases of syphilis under arsenical treatment, who suffered in addition from gonococcal arthritis, the response to treatment by vaccines has been particularly good.

In three cases of very severe polyarthritis with a general septicæmia and extensive keratodermia, we have found that minute intravenous injections of *neo-kharsivan* 0·025 to 0·05 gm., administered every second or third day, have appeared to increase the patient's defensive mechanism and helped very materially to combat the septicæmia prior to administering a course of vaccine therapy.

REFERENCES TO LITERATURE

(1) MARTINIÉRE: *Traité de la Maladie Vénérienne*, 1664.
(2) SALLE, T., and SWEDIAUR: Quoted by A. Thomas, *J.A.M.A.*, p. 2174, December 24th, 1927.
(3) BRODIE, B.: "Pathology and Surgery," 1st Edition., 1818, quoted by Brodie, M. W., *Practit.*, **88,** p. 34, 1912.
(4) NEISSER, A.: *Centralblat F. d. Med. Wissenschaft.*, **XVII,** 497, 1879.
(5) LAWRENCE, W.: Quoted by McDonagh, "Venereal Diseases," p. 313, 1920.
(6) PETRONE: *Rev. Clin. di Bolivia*, 1883.
(7) HEWES: *Med. and Surg. Jour.*, Boston, 1894.
(8) OSLER, W.: "Principles and Practice of Medicine," 9th Edition, p. 127, 1920.
(9) LUMB, N. P.: "Gonococcal Infection in the Male," p. 151 (Bale, Sons & Danielson), 1920.

(10) KLOSE, H. : *Berlin Klin. Woch.*, Vol. **XVI.**, 42, p. 983, 1919.
(11) IRELAND : Quoted by A. Thomas, *J.A.M.A.*, p. 2174, December 24th, 1927.
(12) CHIARI : *Centralbl. f. Grenzgeb. d. med. u. chir. Jena*, p. 445, 1914.
(13) HARRISON and POLLOCK : Quoted by A. Thomas, *J.A.M.A.*, p. 2174, December 24th, 1927.
(14) THOMAS, A. : *J.A.M.A.*, p. 2174, December 24th, 1927.
(15) THAYER and BLUMER : *Arch. de Med. Exper. et d'anat. path.*, Paris, November, 1895 ; also *Johns Hopkins Hosp. Bull.*, Vol. **VII.**, p. 57, 1896.
(16) UYSING : *Inaug. Dissert. Kiel*, 1908 ; quoted by Hunter, *Brit. Med. Jour.*, March 11th, 1905.
(17) ZIELER, K. : *Mediz. Klinik.*, February 11th, 1912.
(18) LOFARO, F. : *Il Polyklinic*, February, 1911.
(19) Quoted by Cole, " Osler's Modern Medicine," Vol. **III**, p. 103, 1907.
(20) NASSE and RINDFLEISCH : *Arch. f. Klin. Chir. u. Samml. Klin. Vortrage*, 1897.
(21) BAUR : *Deut. Med. Woch. Vereinsber.*, p. 60, 1901.
(22) THOMSON, D. : " Gonorrhœa " (Oxf. Med. Publ.), p. 224, 1923.
(23) MCDONAGH, J. E. R. : " Venereal Diseases," p. 313, 1920.
(24) MICHEL, L. L. : *New York Med. Jour.*, p. 1124, June 28th, 1919.
(25) LUCAS, C. : *Lancet*, p. 250, January 28th, 1899.
(26) JOHNSTONE : *Amer. Jour. Dis. of Children*, February, 1921.
(27) FISCHER, M. : *Monatschr. f. Kinder. Leipsig.* 29, October 10th, 1924.
(28) PRITZI : *Wien. Klin. Woch.*, **37**, 1312, December 18th, 1924.
(29) HERZFELD, G. : *Trans. Med. Chir. Soc. Edin.*, January 21st, 1925 ; *Brit. Med. Jour.*, p. 365, February 21st, 1925.
(30) NORTHUP : Quoted by Young, " Manual of Orthopædic Surgery," p. 529, Philadelphia, 1905.
(31) LUMB, N. P. : " Gonococcal Infection in the Male," p. 151 (Bale, Sons & Danielson, London), 1920.
(32) YOUNG, H. H. : *Johns Hopkins Hosp. Reports*, Vol. **IX.**, p 677.
(33) THOMSON, D. : " Gonorrhœa " (Oxf. Med. Publ.), pp. 295 *et seq.*, 1923.
(34) WILSON, FORBES and SCHWARTZ : *Jour. of Immunology*, Vol. **111**, No. 2, March, 1923.
(35) HORDER, T. : *Lancet*, p. 1304, June 30th, 1923.
(36) BESANÇON, WEIL and RUBENSTEIN : *C. R. Soc. de Biologie*, p. 235, July 3rd, 1925.
(37) THOMAS and IVY : *Arch. of Int. Med. Chicago*, Vol. **13**, No. 1, January, 1914.
(38) OSMOND, T. E. : *Lancet*, p. 1304, June 30th, 1923.
(39) BREWSTER, G. : *M. D. Thesis. Edin. Univ.*, 1927.
(40) LUYS : " Gonorrhœa," 2nd Edition (trans. by Foerster), 1917.
(41) PLISSON, L. : *Le Progrès Méd.*, p. 1543, October 1st, 1927.
(42) HORDER, T. : *Lancet*, pp. 1304, 1313, June 30th, 1925 ; *Lancet*, p. 18, July 7th, 1923.
(43) BODENSTAB, R. : *Deutsch. Arch. F. Klin. Med.*, 159, 129–256, March, 1928.
(44) KISSMEYER, *Brit. Jour. of Ven. Dis.*, Vol. **IV.**, p. 199, 1928.

(45) BELFIELD, W. T.: *J.A.M.A.*, **XLIV.**, p. 1277, 1905; **LIX.**, p. 1419, 1912; **LXI.**, p. 1867, 1913; *Surg. Gyn. Obst.*, **III.**, p. 656, 1906; **XVI.**, p. 569, 1913.
(46) BELFIELD, W. T.: *J.A.M.A.*, **LXXIV.**, p. 148, 1920; **LXXVIII.**, p. 1290, 1922.
(47) THOMAS, A.: *Surg. Gyn. Obst.*, **XXIV.**, p. 68, 1917.
(48) KIDD, F.: *Lancet*, p. 213, August 4th, 1923.
(49) WOLBARST, A. L.: "Gonococcal Infection in the Male," 2nd Edition, p. 232 (H. Kimpton, London), 1930.
(50) BELFIELD and ROLNICK: Quoted by Wolbarst, *ibid.*, p. 234.
(51) LOWSLEY: *New York Med. Jour.*, May 4th, 1921.
(52) THOMAS, A.: *Surg. Gyn. Obst.*, **XXIV.**, p. 68, 1917.
(53) MICHEL, L.: *New York Med. Jour.*, June 28th, p. 1124, 1919.
(54) FREIBERG, A. H.: *J.A.M.A.*, Vol. **89,** No. 26, p. 2177, December 24th, 1927.
(55) CUNNINGHAM, J. H.: *Surg. Gyn. Obst.*, **XXXII.**, No. 6, p. 501, June, 1921.
(56) GREENBERG, G.: *Med. Jour. and Record*, **76,** July 21st, 1927.
(57) STELLWAGON, T. C., and MCCAHEY, J. F.: *Jour. of Urol.*, **18,** p. 1, July, 1927.
(58) TOWNSEND, T. M.: *Trans. Amer. Urolog. Assoc.*, 1917.
(59) BAETZNER: *Med. Welt. Berlin*, **IV.**, 250, Berlin, 1930.
(60) COLLINS, C. W.: *J.A.M.A.*, p. 1789, December 3rd, 1921.
(61) CUMBERBATCH and ROBINSON: "Treatment of Gonococcal Infections by Diathermy" (Heinemann), 1925.
(62) PELOUZE, P. S.: "Gonococcal Urethritis," p. 160 (W. B. Saunders), 1928.
(63) VAN PUTTEE, F. J.: *Acta Derm.-Ven.*, Stockholm, **7,** p. 358, June, 1926.
(64) KOVACS, R.: *J.A.M.A.*, Vol. **89,** No. 24, p. 2177, December 24th, 1927.
(65) COYON, A., and GAGEY, J.: *Bullet. Soc. de Therap.*, Mar. 12th, 1924.
(66) O'CONOR, J.: *Lancet*, p. 1585, December 9th, 1899.
(67) KLOSE, H.: *Berlin Klin. Woch.*, October 20th, 1919.
(68) HARRISON, L. W.: "Manual of Venereal Diseases," p. 260, 1920.
(69) KNAUER: *Lancet*, p. 1262, June 13th, 1925.
(70) BARZY: *Bullet. et Mém. Soc. Chir. de Paris*, p. 888, June 27th, 1922.
(71) MOBITZ, W.: *Münch. Med. Wochnschr.*, **67,** pp. 843–844, 1920.
(72) DUFOUR, THIERS, and ALEXEWSKY: *Jour. de Méd. et de Chir. Prat.*, February 10th, 1922.
(73) BALLENGER and ELDER: *Surg. Gyn. Obst.*, **XXXIII.**, p. 574, November, 1921.
(74) CHURCHMAN, I. W.: *J.A.M.A.*, p. 1047, April 13th, 1918; p. 583, August 28th, 1920.
(75) WALTHER, H. W. E.: *Boston Med. and Surg. Jour.*, Vol. **170,** No. 15, 1914.
(76) FREIBERG, A. H.: *J.A.M.A.*, p. 2177, December 24th, 1927.
(77) PLISSON, L.: *Le Progrès Med.*, p. 1543, October 1st, 1927.
(78) KLAPP: Quoted by Axhausen, *Klin. Woch.*, No. 16, 1927.

(79) RAMOND, F., JANET, and LEVY, M.: *Bull. et. Mém. Soc. Méd. d. Hôp. de Paris*, **39,** 200, February 15th, 1923.
(80) WALTHER, H. W. E.: *Loc. cit.*
(81) MONDOR, H.: *Les Arthrites Gonococciques* (Masson et Cie., Paris), 1928.
(82) THOMSON, D.: "Gonorrhœa" (Oxf. Med. Publ.), p. 328, 1923.
(83) CRUVEILHIER, L.: *Lancet*, Vol. **II.,** p. 1311, November 8th, 1910.
(84) BROUGHTON-ALCOCK, W.: *Comptes rend, des Sciences de la Soc. Biol.*, Vol. **74,** p. 623, 1913.
(85) HAWORTH, H. D.: *Brit. Med. Jour.*, Vol. **1,** p. 4, January 5th, 1918.
(86) DOPTER and PAURON: *Brit. Med. Jour.*, Vol. **II.,** p. 1609, 1913.
(87) THOMSON, D.: *Lancet*, **1,** p. 1102, 1919; *Science and Progress*, Vol. **14,** No. 54, p. 326, 1919; "Gonorrhœa" (Oxf. Med. Publ.), p. 335, 1923.
(88) LEES, D.: *Lancet*, **1,** p. 1107, 1919; *Edin. Med. Jour.*, August, 1919.
(89) FRASER, A. R., and DUNCAN, A. G. B.: *Lancet*, p. 248, January 31st, 1920.
(90) SIEUR: *Bull. et Mem. Soc. de Chirug. de Paris*, October 25th, 1921.
(91) LIAN, C., POINCLOUX, P., and COPELOVICI-COPE, M.: *Gaz. des Hospitaux*, p. 1086, July 27th, 1929.
(92) VALLINO, M. T., and MACERO, J. M.: *Semana Medica*, Buenos Aires, **36,** p. 164, January 17th, 1929.
(93) SEZARY, A.: *Compt. rend. Soc. de Biol.*, Paris, **82,** p. 111, 1919.
(94) MICHEL, L.: *New York Med. Jour.*, June 28th, 1929.
(95) ROHRBACH, E.: *Dermat. Zeitschr.*, Vol. **XIX.,** 1912.
(96) DORN, F.: *Dermat. Woch.*, Vol. **54,** 1912.
(97) BRUCK, C.: *Kolle Wassermann*, Vol. **IV.,** 1912.
(98) BARDACH, K.: *Münch. Med. Woch.*, No. 47, 1913.
(99) MARTIN FISCHER: *Monatschr. f. Kinder. Leipsig*, 29, **10,** October 10th, 1924.
(100) FREUND, W. P.: *Wien. Med. Woch.*, No. 25, 1913.
(101) PRITZI, O.: *Wien. Klin. Woch.*, **37,** 1312, December 18th, 1924.
(102) HAGEN, F.: *Med. Klin. Berlin*, Vol. **8,** No. 7, 1912.
(103) ROTH, KLINGER and OPPENHEIM: Quoted by D. Thomson, "Gonorrhœa," p. 315, 1923.
(104) HABERMANN: *Münch. Med. Woch.*, February 24th and March 3rd, 1914.
(105) HARRISON, L. W.: *Lancet*, Vol. **II.,** p. 1375, 1913.
(106) THOMSON, D.: "Gonorrhœa" (Oxf. Med. Publ.), p. 352, 1923.
(107) TORREY, J. C.: *J.A.M.A.*, p. 261, January 27th, 1906; *Med. Record*, New York, October 26th, 1907.
(108) TORREY, J. C., and RODGERS: *J.A.M.A.*, Vol. **49,** p. 918, 1907.
(109) PORTER, F. J. W.: *Lancet*, Vol. **II.,** p. 1479, 1907.
(110) LOUIS: *Trans. Lond. Med. Soc.*, March 15th, 1910.
(111) STEELWAGEN, T. C.: *Therapeutic Gazette*, Detroit, April, 1910.
(112) BALLENGER, S. C.: *New York Med. Jour.*, 1909.

(113) FLETCHER, L.: *Wisconsin Med. Jour.*, reference *Monatschr f. Dermat.*, No. 1, 1911.
(114) BRUCK, C.: *Deutsch. Med. Woch.*, Vol. **35,** p. 470, 1909; *Kolle Wassermann*, 2nd Edition, Vol. **IV.,** pp. 721–736, 1912.
(115) HERBST, R. H.: *J.A.M.A.*, p. 1678, May, 1908; *Illinois Med. Jour.*, Vol. **13,** p. 689, 1908; *Amer. Magaz., N.Y.*, August, 1910.
(116) THOMAS, B. A.: *J.A.M.A.*, Vol. **54,** pp. 258, 362, 1910.
(117) DEBRÉ, R., and PARAF, J.: *Presse Médicale*, Vol. **21,** p. 1013. 1913; *Compt. Rend. Soc. de Biol.*, December 6th, 1913; *Bull. de la Soc. Méd. des Hôp.*, Paris, Vol. **43,** No. 30, p. 908, 1919.
(118) LANGERON and BOCCA: *Lyon Chir.*, June, 1930.
(119) SOLTAU, FENWICK and PARKINSON: *Med. Chir. Arch.*, London, 1906.
(120) FOX, F.: *Brit. Med. Jour.*, Vol. **I.,** p. 979, 1906.
(121) SALTER, A. G.: *Austral. Med. Gaz.*, Sydney, June, 1910.
(122) MALLETERRE, F.: *New York Med. Jour.*, Vol. **103,** No. 22, 1906.
(123) CHIARI, O. M.: *Centralb. f. Grenzgeb. d. Med. u. Chir. Jena*, Vol. **18,** No. 5, 1914.
(124) RAMOND, L.: *Médicin. Paris*, Vol. **III.,** No. 2, p. 154, 1921.
(125) BALLENGER and ELDER: *Surg. Gynec. and Obstet.*, **XXXIII.,** p. 574, Nov., 1921.
(126) THOMAS, A.: *J.A.M.A.*, p. 2174, December 24th, 1927.
(127) RODRIGUEZ, M.: *Paris Méd.*, 63, p. 434, November 26th, 1927.
(128) MCDONAGH, J. E. R.: "Venereal Diseases" (Heinemann), p. 318, 1920.
(129) YOUNG, A.: Quoted by A. I. Wolbarst, "Gonococcal Infection," 2nd Edition, 1930, pp. 92 and 136.
(130) BRASH and BUMPUS: *Ibid.*, p. 92.
(131) YOUNG, A., and YOUMANS, J. B.: *J.A.M.A.*, 87, pp. 746–752, September 4th, 1926.
(132) SMITH, MILLARD: *J.A.M.A.*, June 9th, 1928.
(133) STEIN, H. C., and TRAUBE, W.: *J.A.M.A.*, p. 1608, May 19th, 1928.
(134) LAMBLIN, J.: *Jour. de Scien. Méd. de Lille*, No. 8, February 19th, 1928.
(135) GIRARD and TRIGHER: *Progrès Médical*, No. 16, April 17th, 1920.
(136) DUROEUX, TANT and BERNARD, R.: *Bruxelles Méd.*, November 15th, 1920.

(*To be continued.*)